

## **YNHHS/YM Statement on SARS-CoV-2 Mutations and Variants (UPDATE)**

*This communication involves a topic that is rapidly changing. The information contained represents the best available information at the time of its release. This document will be updated monthly, or sooner if any major event or change requires it.*

SARS-CoV-2 is the virus known to cause coronavirus-19 disease (COVID-19). The SARS-CoV-2 RNA genome has approximately 30,000 nucleotides that encode 29 genes. Viruses develop genetic mutations as they reproduce in the host cell. While numerous SARS-CoV-2 variants have been identified, only a small proportion are of public health significance at this time. Many of the SARS-CoV-2 variants (including all of the CDC's 'variants of concern') contain mutations that alter the amino acid sequence of the receptor binding domain of the spike protein. The spike protein is important as it binds the virus to the host cell receptor (ACE2) and mediates virus entry in the host cell. Neutralizing antibodies, induced by natural infection or vaccination, bind to the spike protein and prevent infection of the host cell.

Fortunately, most variants are NOT associated with resistance to medications, changes in the effectiveness of vaccines, changes in the severity of clinical disease, or the ability to detect or test for the presence of virus. Variants of clinical significance are [classified into three classes by the CDC](#); listed in order of increasing seriousness, they are: 1) variants of interest (VOI), 2) variants of concern (VOC), and 3) variants of high consequence (VOHC). All are monitored and characterized by the CDC and the predicted attributes (i.e. effect on spread, treatments, vaccines) are also listed. There are no current variants of high consequence. A variant of concern is variant for which there is evidence of an increase in transmissibility, more severe disease (increased hospitalizations or deaths), significant reduction in neutralization by antibodies generated during previous infection or vaccination, reduced effectiveness of treatments or vaccines, or diagnostic detection failures. At the time of this document's issue, there are 5 variants of concern.

This situation is being carefully monitored by Yale University and Yale New Haven Health clinicians, scientists, epidemiologists, and laboratories. In collaboration with Yale School of Public Health and CT Department of Public Health, YNHHS is helping to monitor the epidemiology of known variants and the appearance of new variants by identifying and submitting samples for genetic sequencing. Information on the local epidemiology of variants is available here: <https://covidtrackerct.com/variant-surveillance/>. It should be noted that there is 1) a reporting lag in this information and 2) a reporting bias as well, in that the samples provided are a select set of samples that include cases of high suspicion as well as randomly selected cases. National information on variant proportions is reported by CDC [here](#).

**Variant sequencing test results will be used by public health authorities for epidemiologic purposes. SARS CoV-2 surveillance sequencing is not intended or approved for clinical management of individual patients; thus results will not be available in standard clinical reporting formats.**

*This statement is based on current information, recommendations, and evidence and will be subject to revision or retraction based on continued monitoring by the Committee.*

In addition to reporting to the local laboratory, cases of vaccine breakthrough **should be reported to CT DPH** by filling out the ‘COVID-19 Vaccine Breakthrough Case Form’ (<https://portal.ct.gov/DPH/HAI/COVID-19-Healthcare-Guidance>) and faxing this form to the DPH at (860)629-6962. Vaccine breakthrough is defined as SARS-CoV-2 RNA or antigen detection in a respiratory specimen collected  $\geq 14$  days after completing the primary series (i.e. final dose) of an FDA-authorized COVID-19 vaccine. Yale New Haven Health is now identifying these cases by cross-referencing lab and vaccine information on our patients and is generating an automated report to DPH. For these cases identified at a lab at YNHHS, the form would not be necessary.

The accuracy of PCR tests done at YNHHS is not currently known to be reduced as YNHHS assays target multiple regions of the viral genome and most do not target the spike gene region where mutations of concern occur. There may be a higher risk for false negative tests for assays performed outside YNHHS that rely on a single gene target, especially if the spike gene is targeted.

It should be emphasized that universal vaccination is the best strategy to reduce virus mutation. So far studies suggest that antibodies generated by authorized vaccines in the US recognize these variants.

Until then, careful adherence to infection prevention measures by maintaining physical distancing ( $\geq 6$  feet), universal masking at work and in the community, avoiding crowds and gatherings, limiting out-of-state travel to essential travel only, and handwashing is even more critical to reduce spread.

FDA is directing policy and recommendations for test developers and users and this advisory will be updated as needed. ([https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-evaluating-impact-viral-mutations-covid-19-tests?utm\\_medium=email&utm\\_source=govdelivery](https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-evaluating-impact-viral-mutations-covid-19-tests?utm_medium=email&utm_source=govdelivery))

For the latest information on COVID-19 variants, consult the CDC website: <https://www.cdc.gov/coronavirus/2019-ncov/variants/index.html>

- COVID-19 Testing Stewardship Committee

#### Other References:

<https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-surveillance/variant-info.html>

Galloway SE, Paul P, MacCannell DR, et al. Emergence of SARS-CoV-2 B.1.1.7 Lineage — United States, December 29, 2020–January 12, 2021. MMWR Morb Mortal Wkly Rep 2021;70:95–99. DOI: [http://dx.doi.org/10.15585/mmwr.mm7003e2external icon](http://dx.doi.org/10.15585/mmwr.mm7003e2external%20icon).

Walensky RP, Walke HT, Fauci AS. SARS-CoV-2 Variants of Concern in the United States—Challenges and Opportunities. JAMA. Published online February 17, 2021. doi:10.1001/jama.2021.2294 <https://jamanetwork.com/journals/jama/fullarticle/2776739>

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